COMPUTATIONAL TARGET PROFILE

SLC35F2

An SLC35 solute carrier for queuine and the anticancer agent YM155, characterised without an experimental structure

SLC35F2 is the high-affinity importer of the micronutrient queuine and, incidentally, of the anticancer agent YM155 — over-expressed in non-small-cell lung cancer, yet structurally dark. No solved structure, an SLC35-like fold inferred from sequence — resolved into a ten-helix topology, a residue-level substrate-cavity hypothesis, post-translational features and a construct plan, computed with Orbion's Astra suite from the sequence alone.

UniProt Q8IXU6 · 374 aa · SLC35 Nucleotide-Sugar-Transporter-Like · IDG tier: Tbio · PDB: none · July 2026

Have your own under-characterised target? Send a UniProt ID to contact@orbion.life for a preview like this one.

At A Glance

Fold	Ten predicted transmembrane helices in the SLC35 (nucleotide-sugar-transporter-like) fold; multi-pass membrane protein; non-enzyme.
Substrate Cavity	A residue-level substrate-cavity hypothesis from AstraBIND (confidence 0.828, HIGH), unclassified — a starting point for docking and cavity mutagenesis, not a validated ligand.
Flexible Regions	Elevated predicted disorder at the cytosolic N-terminus (1–29) and C-terminal tail (341–373) — natural truncation boundaries for construct design.
Clean Signal	One aggregation-prone segment flagged (AstraUNFOLD amyloid max 0.511) — worth screening in construct design.

PREDICTION CONFIDENCE

Figure 1. Model-reported confidence for the headline calls (amber = load-bearing / soft prediction).

1 The Gap

Most tractable membrane-transporter families have been structurally explored. SLC35F2 has not: an IDG Tbio solute carrier with no experimental structure in the PDB and, until recently, no assigned substrate. That substrate is now identified — SLC35F2 is a high-affinity plasma-membrane importer of queuine and queuosine, bacterially derived micronutrients from diet and the gut microbiome that are incorporated at the tRNA wobble position to support efficient translation. Its oncology interest is better established than its structure: SLC35F2 is the route by which the anticancer agent YM155 (sepantronium) enters cells to do its DNA damage, it is over-expressed in non-small-cell lung cancer — with transcript levels modestly tracking pathological staging — and its degradation confers YM155 resistance.

The gap is structural, not biological: everything below is computed from the canonical 374-residue sequence with Orbion's Astra suite, with no experimental SLC35F2 structure used as input. For a transporter with real oncology traction and no solved fold, prediction is the place to start.

2 Architecture And Topology

PREDICTED ARCHITECTURE

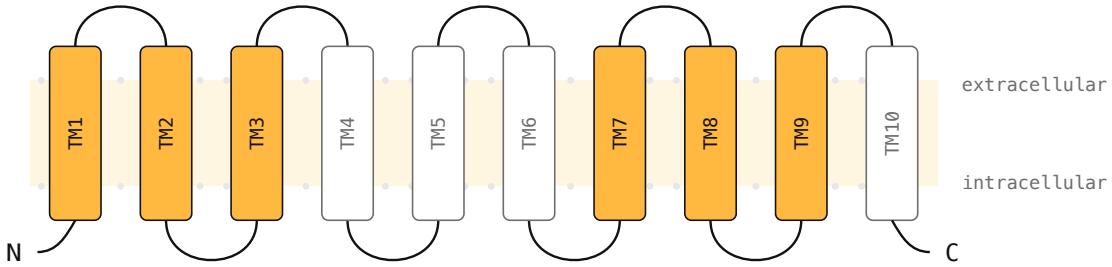

Figure 2. Predicted membrane topology from the sequence: transmembrane helices drawn in the bilayer, amber marks the pocket-lining helices, dashed loops are disordered, and the N/C termini and key modifications are placed in situ.

Element	Residues	Note
Transmembrane Helices	10 predicted	Boundaries: 39–59; 73–93; 108–125; 136–156; 165–185; 195–215; 227–247; 263–283; 291–311; 314–334.

PER-RESIDUE DISORDER PROFILE (ASTRAUNFOLD)

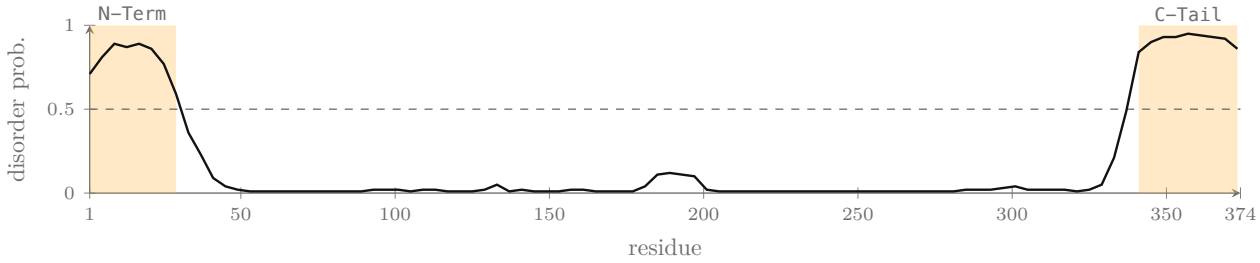

Figure 3. Predicted per-residue disorder (dashed = 0.5 call threshold); amber bands mark flexible regions — natural construct / truncation boundaries.

3 The Predicted Substrate Cavity

Astra resolves a residue-level site — the input a docking run or a mutagenesis plan actually needs. Predicted location: **Predicted central translocation cavity**.

PREDICTED POCKET / FUNCTIONAL RESIDUES

TM1	52–53
TM2	75, 77, 79–80
TM3	118
TM7	229, 231–233
TM8	268, 270, 272, 275–277
TM9	295

For this genuine orphan, AstraBIND has no ligand-bound relative to retrieve from — so these residues are a structure-based cavity prediction, not a retrieval-grounded pocket, and the score reflects cavity geometry rather than a known binding site. Treat them as an exploratory starting point for mutagenesis only; the topology, disorder and modification maps above are the higher-confidence outputs for this target. No validated ligand; not a proven druggable site.

4 Post-Translational And Structural Features

- **Aggregation-prone segment flagged** (AstraUNFOLD amyloid max 0.511) — a predicted amyloidogenic stretch to screen out or engineer around in construct design.

5 Recommended Experimental Follow-Up

Prediction	Experiment	Readout
Substrate-Cavity Residues (TM2, TM7, TM8)	Cavity-lining alanine scan + queuosine or YM155 uptake assay	Loss of transport at the predicted site
Disordered N-Terminus and C-Tail (1–29, 341–373)	Terminal truncation or fusion-partner insertion	Improved expression / thermostability for structural work
Predicted SLC35 Transporter Class	Queuine/queuosine or YM155 uptake in a defined cell system	Confirm transport function and substrate selectivity

6 Where This Fits In A Discovery Workflow

Team	What they get from this profile
Target Biology	Testable residue-level hypotheses and a validation plan
Structural Biology	Construct boundaries, disordered regions, fusion / deletion ideas
Medicinal Chemistry	Pocket / active-site residues for docking and SAR
BD / Platform Evaluation	Evidence Orbion can prioritise dark targets quickly

7 Methods

All predictions were generated with Orbion's Astra suite from the canonical SLC35F2 sequence (UniProt Q8IXU6): **AstraSUIT** and **AstraROLE** (membrane / functional class), **AstraUNFOLD** (topology, disorder, aggregation), **AstraPTM** (modification sites) and **AstraBIND** (binding pocket). Reported values are model outputs; model internals are out of scope. No experimental SLC35F2 structure or ligand was used as input. Predictions are computational hypotheses to prioritise experiments, not validated results.

8 References

1. UniProt Consortium. UniProtKB entry Q8IXU6 (SLC35F2, human). uniprot.org.
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4. Bu L et al. Highly expressed SLC35F2 in non-small cell lung cancer is associated with pathological staging. (2011). https://doi.org/10.3892/mmr.2011.572
5. Chandrasekaran AP et al. USP32 confers cancer cell resistance to YM155 via promoting ER-associated degradation of solute carrier protein SLC35F2. (2021). https://doi.org/10.7150/thno.63806